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Editorials . . .

THE DOCTOR AND HIS GOVERNMENT

At present there are several proposals before our Congress recommending legislation for a nation-wide health program, firmly establishing a government interest in the education of physicians, the care of patients and other matters which heretofore have been recognized as the exclusive domain of the medical profession. Many members of the profession have risen on their heels and are now loudly arguing against such a program, proclaiming that the government is superceding its rights in entering the field of medicine.

Actually, the contemplated measures are but logical outgrowths of a governmental interest in the health of the nation which has been growing for almost a century. In the early days of our history, the community charges — sick in mind or body or poverty-stricken — were looked upon with contempt, and those officials charged with their care were the most incompetent members of the political family of grafters. In the latter half of the 19th century, the public attitude changed to one of sympathy and understanding and the welfare of those unable to care for themselves became an important phase of government. Agencies were established, utilizing trained personnel, which eventually covered the fields of child and maternal welfare, unemployment and compensation relief, old age pensions, etc. One of the most respected and necessary fields of public welfare—one from which all citizens, wealthy as well as indigent, benefit — is that of public health.

Public health has remained one of the chief concerns of the government. Health departments exist at local, state and national levels. Inspections of water purity, sanitary and sewage conditions, safety of housing, adequacy of heat, light and air in working places — all of which are important to the health of the people — are now accepted duties of the government. More directly, the government has accepted the responsibility for the care of the mentally ill in state hospitals, for veterans in federally run institutions, for the health of children in public schools, for the prevention of tuberculosis, for the quick discovery and treatment of venereal disease. During the past war, the federal government used the medical schools to train physicians for the armed forces, and at present, many states are offering scholarships to medical schools to those men who would return to rural areas after the completion of their studies. Physicians may forget that the police power of the political state backs up the quarantine of contagious diseases — and also protects the practice of the physician from the competition of unqualified quacks.

Rather than fight government "intervention" in medicine as such, the individual physician must be realistic. Government is already an integral part of medicine as it is practiced in this country and no doctor

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would wish it otherwise in most cases. Many physicians actively cooperate with the government by taking office in local health departments or deserting more lucrative fields of activity by taking a rather poorly paid career in the public health service.

It is up to the individual physician to analyze carefully each instance where government "intervention" is proposed for the medical profession. He should fight for such intervention in certain situations (grants for research, hospitals for backward areas, subsidies for needed medical care, etc.) as vehemently as he attacks intrusion in others. His decisions should be based on his knowledge as an expert and not on his prejudices as a private interest.

THE USE AND ABUSE OF PENICILLIN

The advent of penicillin together with the other antibiotics marks a historical change in the practice of medicine — a change which has the mark of a double-edged sword. Many infectious diseases which previously had a high fatality rate and which could only be treated symptomatically now have specific therapy thereby reducing the mortality and morbidity many-fold. On the other hand, many physicians, overlooking the fact that penicillin is specific, abuse the double-edged sword by using it as a shotgun cure. Their belief in the power of the drug is so prevailing that they tend to utilize it in any and every case of fever. Their clinical judgment becomes slack; diagnoses are no longer made. Penicillin now makes the diagnosis.

Antibiotics are, of course, definitely indicated in those cases where infection is obviously the source of fever — as in cellulitis, suspected osteomyelitis or pneumonia, or where secondary infection is feared. In these cases, where speed is of great importance, no one would wait to institute therapy until bacterial cultures and other laboratory tests are made any more than one would wait for the return of a positive EKG before treating myocardial infarction. Still, confirmation of the clinical diagnosis should be sought by laboratory tests.

It is in those cases where the nature of fever is not apparent at first that the use of penicillin should wait until a positive diagnosis, based on a complete laboratory work-up, has been made.

It is good medicine to make a diagnosis before instituting therapy; or, to put it another way, "Treatment should be based on the patient's ills." This old maxim, taught in the first years of medical school, is so often forgotten for the sake of convenience. When no diagnosis is made and penicillin is instituted for a disease refractory to the drug, the disease remains untouched to continue its destruction. The physician, lulled by the sense of security he gains from the use of antibiotics, learns much later that the disease is still present and awaiting treatment. Fever, per se, has never killed anyone, but the underlying cause has; and the physician may be deluding himself and his patient when he combats the fever alone without a thorough investigation of the underlying cause.

THE DIAGNOSIS AND TREATMENT OF CONGESTIVE HEART FAILURE

HARRY J. ISAACS, M.D.*

IT IS a well known fact that dyspnea is the most important symptom of cardiac failure and that that symptom alone attracts the attention of the clinician. Still there are many patients who complain of the above, that we encounter in our everyday practice of medicine, who do not have any clinical evidences of cardiac disease. The obese patient is especially in this classification, complaining markedly of dyspnea on the slightest effort; though the underlying pathology is non-cardiac. The correction of the obesity is the only therapy necessary. Again we see patients complaining of difficulties in breathing, who state that they have to take real deep and rapid breaths to get enough air in their system. These patients are also non-cardiacs and fall in the classification of neurosis or functional conditions. Their co-called dyspnea associated with deep sighing and respirations are due to hyper-ventilation of the lung. The therapy directed toward this complaint rests with the psychiatrist.

The dyspnea associated with pulmonary conditions (acute or chronic) is well known and it is the usual picture to see the chronic emphysematous patient; the spontaneous pneumothorax case; the carcinoma of the lung or the mediastinal pathology complain of dyspnea. In addition, anemia from whatever cause, is a marked factor in the production of dyspnea. Therefore, as clinicians, we try to interpret our symptoms properly, remembering, however, that the most common cause of dyspnea is still cardiac failure.

For practical purposes we can divide heart failure into left and right heart involvement. Left heart failure is characterized by maximum dyspnea and orthopnea and minimum cyanosis, while right heart failure presents the symptoms of minimum dyspnea and orthopnea and maximum cyanosis. It is well understood by all that left heart failure is characterized by pulmonary congestion and that right heart failure by systemic congestion. The earliest complaint of left heart failure may be irritability, restlessness, fatigue and sleeplessness and inability to concentrate, before the true dyspnea presents itself. This dyspnea may only be present with the slightest exertion.

The other symptoms and findings of left heart failure are nocturnal dyspnea, orthopnea, Cheyne-Stokes breathing, pulsus alternans, gallop rhythm, accentuated second pulmonic sound, rales at the bases (right base first), hemoptysis, pulmonary edema and decrease in the vital capacity. One of the earliest symptoms of left heart failure is nocturnal dyspnea. This occurs usually in the degenerative, arteriosclerotic or coronary type of heart disease, and is rare in rheumatic heart disease, unless a high grade button-hole stenosis or an associated rheumatic aortic regurgitation is present. The exact mechanism is not understood very well, but it is thought to be due to accumulation of metabolites at night which stimulate the respiratory center. From a practical point of view many patients present themselves with the statement that during the day they have little or no complaints, but at night they are awakened from a sound sleep complaining of heaviness and discomfort of the chest with difficulty in breathing, which necessitates them getting out of bed and walking about for a while, until they get relief. Many of these patients have wheezes and rales in their chest at that time and a diagnosis of bronchial asthma is made. If one remembers that allergic asthma is a disease of youth and is quite chronic in character, and that nocturnal dyspnea occurs in the older (arteriosclerotic) group and usually is very recent (a week or more) in origin. Adrenalin is contra-indicated in nocturnal dyspnea for the arteriosclerotic or coronary patient, for the administration of the drug may precipitate an attack of acute coronary thrombosis. It is also of interest to note that when this patient presents himself to the physician the next day there may be no physical findings whatsoever.

The three important findings, which usually denote a severe condition of left heart failure, which may occur singly at times, are Cheyne-Stokes breathing, pulsus alternans, and gallop rhythm. These may occur with a dry lung (no pulmonary rales) and it is baffling at times to see a patient with the above symptoms and find-

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ings and still be free of rales. One knows that Cheyne-Stokes breathing can also occur in cerebral pathology, and it is quite common to see severe cardiacs who have the above symptoms or only Cheyne-Stokes breathing treated as cerebral cases.

The accentuation of the second pulmonic sound is a common finding in left heart failure and it is interesting to watch the progress being made when cardiac therapy is instituted. As compensation occurs, the second pulmonic sound gets less intense and the second aortic sound becomes more pronounced. If right heart failure ensues, the P_2 becomes diminished, and when the right heart findings disappear, and only left heart manifestations are present, the P_2 again becomes accentuated. Thus, one can watch the progress of a given heart case by the simple procedure of comparing the P_2 with the A_2 and noting the intensity of the second pulmonic sound.

Rales, dependent in position, occurring always at the right base first, are one of the most important physical findings of left heart failure. As time and failure progress (more marked), one can hear rales also in the left base. The presence of rales only in the left base speaks against heart disease, and may occur in a pneumonia, bronchiectasis or a left basal atelectasis due to a carcinoma. Definite progress of the heart case can be determined by the simple procedure of auscultation of the chest. It is interesting to note that many elderly patients have a low grade atelectasis or a chronic bronchitis and that the persistence of basal rales in the presence of better feeling and improvement of the patient has no significance whatsoever. The final judgment in regard to the interpretation of these rales rests with the clinical judgment of the internist. As a clinician, I would like to point out that chronic low grade left heart failure can occur, which may last months or even years. These patients complain of a chronic cough which simulates closely that of a chronic bronchitis. I have seen elderly patients who complain of a chronic cough for months, who show a few basal rales, and who are treated with one or the other cough mixture. They present themselves purely for relief of their chronic cough, with the statement that they have taken many bottles of one or the other cough mixture and have obtained no relief. The addition of digitalis preparation usually solves their problem. It is of interest to note that the rapid disappearance of rales can only occur in left heart failure or in a case of atelectasis and that pulmonary pathology per se causes a gradual or much slower disappearance of the rales. This is an important observation, because at times heart failure may be treated for a pneumonic process or vice versa. Left heart failure with its pulmonary congestion is antagonistic to diseases of the lungs such as pulmonary tuberculosis or pneumonic processes. It is a well-known fact that right heart failure in congenital hearts is often associated with lung tuberculosis. On the other hand it is not uncommon to see a rheumatic mitral stenosis with cardiac failure (left) causing brown induration of the lungs affecting only the apex or both apices, with the physical findings of dullness and rales over both apices which simulate a pulmonary tuberculosis. If one remembers that pulmonary tuberculosis and mitral stenosis are antagonistic diseases and that mitral stenosis at times can cause congestive (chronic) manifestations at the lung apices, one will never make an additional diagnosis of pulmonary tuberculosis in the frank case of rheumatic mitral stenosis, unless one obtains a positive sputum for tubercle bacilli or definite evidences of cavity formation are present.

Hemoptysis is a common finding in left heart failure, occurring in mitral stenosis, pulmonary edema and also in lung infarcts. At times one is confused as to whether or not the hemoptysis is cardiac in origin. The sending of the sputum to the laboratory for evidences of heart failure cells, clinches the diagnosis of cardiac disease.

Cardiac murmurs usually play an important role in the diagnosis of heart failure. One must remember that at times a systolic murmur may be functional in character, and that diastolic murmurs are organic. During extreme cardiac failure, it is often difficult to time the murmur.

The pulse aids us considerably in the determination of heart failure, for a rapid or irregular pulse, such as in auricular fibrillation, gives us more substantiating evidences of heart involvement. At times heart disease is encountered at the onset, with shock and collapse. There are only a few cardiac conditions associated with the above; these being acute coronary thrombosis, acute pulmonary infarcts, or at times a dissecting aortic aneurysm.

Right heart failure is characterized by minimum dyspnea and orthopnea, with maximum cyanosis; this being due to a decrease in the pulmonary congestion and a marked increase in the systemic congestion. The prominent symptoms and findings are dependent edema, enlarged tender liver, ascites, hydrothorax, increase in venous pressure; jugular pulsation, expansile pulsating liver, and a hepato-jugular reflux. Various gastro-intestinal symptoms, such as nausea and vomiting may be present. The urinary output is decreased and albumin may be present in the urine due to passive congestion of the kidney. The urine may show a high fixed specific gravity in contradistinction to primary kidney pathology which shows a low fixed specific gravity. Orthostatic oliguria is a common finding in heart failure. I have seen many cases of heart failure associated with an extrarenal azotemia, simulating a chronic uremia. However, in these cases the N.P.N. may reach 100 mg per 100 cc of blood, but the blood creatinine remains around normal (1—1.5 mg). This disproportion between the N.P.N. and the creatinine speaks for a heart condition and not a primary kidney syndrome. In these heart cases one can use the organic mercury preparations freely and as compensation ensues the extrarenal azotemia disappears.

It is of interest to see a case of extreme left heart failure with its marked dyspnea and orthopnea, who has had the gamut of therapeutic procedures with no response whatsoever, and who is unable to breathe, sleep or eat; to find that at at some later date this patient can lie comfortably in bed and breathe with more or less ease. This type of case has developed a superimposed tricuspid regurgitation (right heart failure) with all its systemic manifestations, and a marked decrease in the pulmonary congestion. That is the reason these patients are comparatively comfortable. When we analyze this type of case we know that the prognosis is decidedly worse, but at least, these patients are alleviated from their symptoms and feel comparatively comfortable. Later, should the right heart compensate, and only the symptoms of left heart failure be present, we again have the return of marked dyspnea and orthopnea. In this type of case, there is usually a good deal of explanations necessary to ease the minds of the relatives of the patient.

The types of heart disease that usually show extreme right heart failure and little or no left heart failure are some of the congenital hearts, chronic Cor Pulmonale, Ayerza's disease and a Bernheim syndrome. This syndrome (Bernheim) is characterized by hypertrophy of the left ventricle with enlarged or hypertrophied interventricular septum which causes obstructive manifestations of the right ventricle and all the characteristic symptoms and findings of right heart failure and no manifestations of left heart failure. Thus, at times, one can have a degenerative heart, with failure, presenting only the symptoms and findings of a right heart.

Edema is a common physical finding in heart disease, very often dependent in position and more marked at the end of the day. However, there are other conditions which can cause edema, such as acute glomerular nephritis, hypoproteinemia; intercapillary glomerular sclerosis (Kimmelstiel-Wilson disease), nephrosis, amyloidosis, pernicious anemia and local pathology of the lower extremities such as pes planus and varicose veins of the leg. It is quite disturbing at times to treat an edema case as a cardiac, only to find out at a later date that your patient has a pernicious anemia or some form of hypoproteinemia. In many of my cases of edema I am interested in the report of the total proteins of the blood with the serum albumin and serum globulin ratio.

A palpable, enlarged, tender liver is the usual finding in right heart failure. The most common cause of enlarged tender liver is cardiac pathology. The more acute the right heart failure is, the more tender is the liver. These patients complain of epigastric distress or pain. As your liver becomes enlarged, a definite hepato-jugular reflux is obtainable. The simple procedure of compressing the liver causes a slight or moderate dilitation of the external (right) jugular. This finding is a definite one for right heart failure and is due to a superimposed functional tricuspid regurgitation. At times, at the bedside, one may quibble as to the cause of the enlarged liver. If a definite hepato-jugular reflux is present, one can rest assured that the liver enlargement is cardiac in origin.

Dullness over the lower sternum occurs in right heart failure. Normally, the upper and lower sternum's are resonant to percussion. Dullness in the upper sternum occurs in aneurysms,

substernal thyroids, upper mediastinal masses (Hodgkins, leukemia or lymphosarcoma) while dullness in the lower sternal region occurs in right heart failure, pericardial effusion and an inferior mediastinal syndrome (tumors).

Hydrothorax and ascites are common physical findings. The hydrothorax occurs first in the right pleural cavity and later involves the left side also. The right sided fluid is due to compression of the azygos vein. If on examination of the chest, left sided fluid is found and none on the right side, it is quite definite that the condition is noncardiac. However, occasionally, from obliteration of the right pleural cavity from some previous disease, such as lung infarcts, pulmonary tuberculosis or pneumonia with its associated pleuritis, the fluid may only occur in the left pleural cavity. Hydrothorax fluid is usually straw-colored, but at times a definite hemorrhagic fluid may be present due to a superimposed lung infarct on that side.

The electrocardiogram may be of some help in the diagnosis of cardiac failure; though the only information one may get are those of the cardiac irregularities, hypertrophy of one or the other ventricles, myocardial degeneration, and a recent or old myocardial infarct. One does not need a EKG to clinch the diagnosis of cardiac failure, for the symptoms and findings are more conclusive. The EKG should only be used as an adjunct in the entire picture.

There are certain basic principles that we all institute in the treatment of heart disease. These are briefly rest, diet and drug therapy. Many hearts respond beautifully to the simple procedure of rest without any other therapeutic procedure. The rheumatic and degenerative hearts seem to respond much better to therapy than do the luetic hearts. The only caution about absolute rest in bed is the tendency some clinicians have of keeping their arteriosclerotic (aged) patients too long in bed, with the resulting complications of broncho-pneumonia and lung infarcts. It is advisable to have more or less free motion of the lower extremities to prevent embolic phenomena to the lungs; for these emboli usually come from the deep veins of the legs and pelvis.

Diet should be wholesome, low in caloric value; salt and sodium free or low in content. Limitation of fluids, I believe, is contra-indicated. Many patients with extreme right heart failure respond to large quantities of fluid. Cases have been reported where diuretic action was obtained with 6-8000 cc of fluid per day, causing a disappearance of the edema. My own personal experience has shown me that I allow my patients to take as much fluid as they desire. It is a common observation that edematous patients respond much better on a hot day when their fluid intake has been markedly increased.

Among our cardiac drugs are the narcotics, digitalis series, or the various glucosides of digitalis, and at times the usage of Squill and Strophanthin preparations. I feel that any digitalis preparation is the drug of choice and the proper use of this drug will result in the maximum therapeutic efficiency. The extract (tablet or pill) is preferable to the liquid digitalis. The dose of digitalis is about 2 grains for every 10 lbs. of body weight. This can be given in one dose in extreme cases (rarely) or in divided doses in chronic cases. Many clinicians give ¼ of the amount for the first dose, ¼ three-quarters of an hour later and the remaining 50% in 12-48 hours. One uses his clinical sense and judgment in giving digitalis. The dosage is the same whether you use the drug orally, hypodermically, intravenously or rectally. The maintenance dosage varies with the individual.

It is a well-known fact that the best results are obtained in the cases of rapid pulse, especially auricular fibrillation, and that the results are not so gratifying in the slow regular pulse. In these slow pulses one has to accentuate the usage of diuretic drugs. Many drug firms inform the clinician that they have a digitalis preparation which causes no toxic manifestations. This, I believe, is incorrect, for any potent digitalis preparation will cause toxic symptoms after the drug has had its accumulative action. I feel that it is a good policy to prescribe your drug until mild toxic manifestations occur; for at least one knows that you have given enough of the drug. Usually too small doses are being given for proper therapeutic effects.

The toxic effects are well known by all, but I would like to mention two untoward effects of digitalis which occur in the arteriosclerotic (aged) group. One syndrome is that of marked mental or psychiatric symptoms which simulate a senile dementia. These patients present none of the symptoms of nausea, vomiting, bradycardia,

dropped beats, extra systoles or pulsus ligninus. The other syndrome presents a persistent diarrhea only; at times even associated with a blood eosinophilia. This syndrome makes you believe that there might be an underlying carcinoma of the bowel. All the above symptoms disappear with stoppage of the drug.

Morphine is a very valuable drug. It is advisable to give ¼ grain at night for sleep for three to six nights. The usage of morphine for sleep causes a very definite improvement of the patient, especially if the patient has not slept for a few nights.

The diuretic drugs play an important role and one may only mention some of these drugs such as the Xanthine derivatives, ammonium chloride and the organic mercury preparations. Therapeutic results with the Xanthine drugs are not so gratifying; however, the best preparations are the organic mercury preparations and the ammonium chloride. I personally use 90-120 grains per day of the ammonium chloride, using the enteric coated tablets. The production of an acidosis results in excellent diuresis. The organic mercury preparations can be used alone or in conjunction with the ammonium chloride. These mercurials can be given intramuscularly or intravenously every second or third day. The maximum dosage for the intramuscular administration is 2 cc and for the intravenous, 1½ cc. It is inadvisable to use the intravenous route in coronary artery diseases. The presence of albumin in the urine is no contraindication for its usage and the administration of this drug for left heart failure alone very often spells the difference between success and failure. The mercurials causes a very rapid disappearance of the pulmonary rales.

Aminophyllin intravenously relieves dyspnea, paroxysmal dyspnea, nocturnal dyspnea and Cheyne-Stokes breathing. This drug can also be given rectally. Oxygen and venesection for cardiac failure is a known therapeutic procedure and morphine for pulmonary edema is par excellence. At times thoracentesis and abdomenal tappings have to be done. If the pleural fluid is up to the angle of the scapula or a moderate amount of fluid is present in the peritoneal cavity, one has to resort to tapping; for diuretic drugs will be of no avail. Occasionally, Southey tubes have to be inserted in the lower extremities for a marked edema. Thus, one can easily see, that with the proper and intelligent use of the various drugs we have at our command, that excellent or good results should be obtained for the cardiac patient. In the early diagnosis and treatment of cardiac failure rests our prognosis.

ORTHOPEDICS COMPLICATED BY VASCULAR IMBALANCE

DONALD S. MILLER, M.D., Ph.D.*

THERE are many orthopedic conditions which are affected unfavorably by a reduction of the peripheral circulation. It becomes important, therefore, before surgery of an extremity is contemplated, to evaluate these findings and treat the extremity accordingly. This will frequently prevent such untoward surgical catastrophes as gangrene, tissue necrosis, skin ulceration following traction and surgery, and various deformities from vascular spasms that may result in a permanent joint condition.

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To avoid such pitfalls in orthopedic surgery patients with various vascular imbalances were subjected to a vascular survey. These surveys included clinical observation (color of the skin, warmth of the limb, palpation of pulses, and color changes following changes in position), oscillometric readings, temperature readings, fluoresceine dye tests, plethysmograph studies, response to the circulation to indirect heat and drugs, and arteriograms.

Although most of these tests are relatively simple and can be done by the practitioner, several — such as plethysmography and arteriography — require some special technical skill. One may see that the simple tests outlined above

are the ones that usually give the most pertinent data as regards circulation of the limb. Most of the tests, too, are qualitative in type; plethysmography is the only test that will actually give a quantitative amount of blood in a portion of an extremity.

Approximately fifty cases were studied during the past year and the following is a sample outline of the vascular responses:

A. Orthopedic Cases with Reduced Arterial Circulation
   1. Gangrene of the extremity
   2. Gangrene due to traction
   3. Ischemia with fibrosis resulting from traction methods.
   4. Aneurysms of the popliteal area
   5. Fractures of the lower third of the leg, complicated by osteomyelitis and ulcer formation.

B. Orthopedic Cases with an Increase of Arterial Circulation
   1. Sudeck's bone atrophy
   2. Causalgia-like extremity
   3. Osteomyelitis of the ankle
   4. Tuberculosis of the ankle.

The treatment of Group A cases is briefly outlined in the following chart.

Treatment of Vascular Orthopedic Cases

a. Prevention of tissue necrosis and gangrene by:
   1. Careful evaluation of circulation
   2. Avoidance of "over-treatment"
   3. Foot hygiene
   4. Careful bandaging in fractures
b. Rest of the extremity
c. Indirect heat, if necessary
d. Vasodilating drugs, as Dibenamine and Etamon
e. Sympathectomy to increase collateral circulation
f. Careful surgery — avoid further damage to collateral circulation
g. Use of antibiotics and sulfa drugs for potential or active infections
h. Conservative treatment of vascular complications in young patients.

Summary and Conclusions

1. It is imperative that all cases with gangrene be subjected to a thorough vascular survey, to investigate the status of the collateral circulation, in order to determine the optimum level for amputation.

2. Orthopedic cases, manifesting signs of an associated organic vascular disease, should be treated pre-operatively by various procedures designed to increase peripheral blood flow, such as indirect body heating to inhibit vasomotor tone locally, vasodilating drugs, paravertebral sympathetic procaine block and sympathectomy. The general condition of the patient must also be studied and treated accordingly.

3. Tight bandages, particularly of the elastic type, should be used carefully in the treatment of fractured femurs in children, especially when Bryant's method of treatment is used.

4. Arterial aneurysms in the extremity, manifesting signs of a poor collateral circulation, should be treated conservatively until it is determined that an adequate blood flow exists, with the aneurysm temporarily obliterated by digital pressure.

5. Tissue necrosis and various types of ulcers should be treated conservatively and generally over a prolonged period of time. Early in their inception, sympathectomy and the use of vasodilating drugs may prove of some benefit.

6. Such cases as Sudeck's bone atrophy and causalgic states respond well to repeated paravertebral sympatheic procaine blocks and sympathectomy.

POLYSACCHARIDES AS HETEROPHILE ANTIGENS*

George J. Scheff, M.D., Ph.D.**

SINCE Forssman's first communication in 1911, (1) the topic of heterophile antigens[1] has outgrown the limits of a brief report of this nature. It will be necessary, therefore, to narrow down the present discussion to three distinct groups of active agents. These are: 1) The Forssman type of antigen in its original meaning; 2) the "A" group specific substance of the RBC's; 3) the heterophile antigens of some bacteria.

All three of these groups have in common the fact that they are chemically speaking, polysaccharides. Simple as it may seem today, this fact was not recognized until recently. This is not surprising, since at the time of Forssman's discovery, the carbohydrates were not believed to be immunologically active substances.

1) *Original Forssman Type Antigen*: Forssman was able to demonstrate that when watery suspension of guinea pig organs were injected into rabbits, a powerful lytic immune body developed which reacted not only with guinea pig cells (as would seem to be consistent with species specificity), but also with sheep red blood corpuscles. Further studies then showed that the tissues of not all animal species are alike in this behavior. There are animals which follow the "guinea pig type," possessing the Forssman antigen (cat, dog, horse, mouse, etc.), and there are others which apparently do not have it and belong to the so-called "rabbit type" (ox, pig, rat, etc.). Similarly, some bacteria are equipped with the Forssman antigen, whereas others are devoid of it. In animals it was observed that if the antigen was present in the organs, it was usually absent from the blood elements, and vice versa (with only a few exceptions on record). Furthermore, it is usually true that heterophile antibodies can only be produced in those animals in which the heterophile antigen is missing from both the organs and blood.

The chemical analysis of the active principle was attended by many failures and it is quite instructive to trace the reasons for these errors. Landsteiner and his associates (2a, 2b), in their earlier work were able to show that the Forssman antigen was extractable with absolute alcohol. The tissue lost thereby its ability to fix the pertinent antibody, while the factor responsible for it could be recovered in the alcoholic residue. The latter, though completely adequate to unite with the antibody in vitro, would not produce antibodies when injected into rabbits. It was assumed, therefore, that somewhere along the line of preparation a splitting had occurred which resulted in the formation of a haptene. Since the material was extractable with alcohol, it was concluded that the haptene is a lipoid.

Following up the idea that the haptene was a split product, attempts were made to regenerate the "complete" antigen by combining the haptene, i.e., the concentrated alcoholic extract of heterophile organs, with an indifferent serum. For this purpose hog serum was used which is free of heterophile antigen. It was found, indeed, that when these two constituents were mixed and allowed to stand before the injection, true Forssman antibodies could be produced in rabbits. Consequently, the deduction was made that the alcohol precipitated the protein moiety which is left behind during the alcoholic extraction and only the lipoidal part went into solution. Later, however, Landsteiner and Levine (2c) were compelled to abandon the original concept. They found that if they left the alcoholic extract in the refrigerator over night, a precipitate formed which carried along the reactive grouping. The precipitate after isolation was no more alcohol soluble but rather easily soluble in water. After purification of the material, a substance was obtained which was practically protein and lipoid free and which behaved like a typical polysaccharide. On acid hydrolysis, the watery solution yielded large quantities of reducing sugars. From this and

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* Lecture delivered at The Chicago Medical School Seminar, November 19, 1947.

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(1) Heterophilic or heterogenetic antigens are defined as heat-stable agents which are capable of stimulating the production of completely unrelated antibodies. The Forssman antigen is presently regarded as one special sub-group which, like guinea pig organs, induce antibodies reacting with sheep RBC's only.

some other evidence, Landsteiner concluded that the Forssman haptene, derived particularly from horse kidneys, is a carbohydrate which is single or in some combination with a lipoid. These findings were supported by the later work of Brunius, who identified the reducing substance of the hydrolized horse kidney antigen as hexosamin. A close parallelism existed between the hexosamin content and the serological activity.

TABLE I.

	C %	H %	N %	Red %	CH_3CO	Serological Activity γ
Human Urine (Freudenberg, (6) 1932-1935)	45.5	5.9	5.4	50.0	9.50	0.010
Horse Saliva (Landsteiner, (2d) 1936)	44.6	6.9	7.1	57.4	9.43	0.00025
Witte-Pepsin (Freudenberg, 1938).....	45.7	7.3	4.8		9.14	0.00006
Hog-Pepsin (Landsteiner, (2f) 1940).....	46.6	6.9	6.0	63.0	12.75	0.0010
Difco-Peptone (Goebel, (7) 1938).....	46.7	6.5	5.9	73.0	9.56	0.010
Pfenstiehl-Peptone (Goebel, 1938).....	44.9	6.2	5.5	62.0	8.90	0.100
Ovarian Cyst (Morgan & King, (8) 1944.....	44.8	6.9	6.0	—	10.00	0.125

Variable amounts of "S" were also found to be present.

2) *"A" Group Specific Substances*: Schiff and Adelsberger (3) were the first to show that human erythrocytes of the "A" group carry antigenic properties similar to those of sheep erythrocytes. Consequently, a rabbit immune serum containing anti-"A" isoagglutinins reacted under proper conditions with the pertinent human erythrocytes as well as with the sheep RBC's. Superficially, this may seem to be analogous to the type of heterogenetic observation made by Forssman, but further experimentation revealed unquestionable differences. Thus, by applying the selective absorption technique, it was demonstrable that human erythrocytes "A" will absorb the anti-sheep cell hemolysins from an anti—"A" human serum, but not from an anti-guinea pig tissue serum (or Forssman serum).

Instead of discussing the existing differences between the two antigens any further, it seems more profitable to search for more easily accessible sources for preparing the "A" substance than the erythrocytes themselves. Some of these are: Human saliva and urine; horse saliva; hog stomach pepsin; and various peptones. As with the original Forssman's antigen, the active principle was first believed to be a lipoid since it was partly extractable with alcohol. Soon, however, Landsteiner and Van der Scheer (2b) demonstrated that the major portion of the active material is left behind after alcoholic extraction. Somewhat later, Brahn and Schiff (4), and Hallauer (5) succeeded in isolating the water soluble portion, and the latter obtained a substance which inhibited the isoagglutination in amounts as low as 1/400 γ. The final purification again established the polysaccharide nature of the active principle.

The purified preparation from various sources showed fair agreement with each other (table 1).

While the elementary analysis is fairly uniform, the reducing power, after hydrolysis and the serological activity is less constant. Among the principal building stones of the "A" substance were found galactose and acetylglucosamin as regular constituents. Further details regarding the composition of the "A" substance were established by Landsteiner and Harte (2f). These authors demonstrated that aside from hexosamin, a substantial portion of the nitrogen is derived from amino acids. They concluded that the active substance might be made up of a new type of a polysaccharide-peptide linkage. However, all the chemical analyses have been far too crude so far, to provide final results, and this explains why on the one hand an amount of .00006 γ and on the other hand. .125 γ are effective.

3). *Bacterial Heterophile Antigens*: Heterophile antigens of bacterial origin were recognized very early in systematically unrelated

organisms, but only after Forssman's discovery were these studied in such orderly manner that they assumed a real meaning. Among the bacteria most commonly studied were S. schottmulleri, Sh. dysenteriae, and Pneumococci.

TABLE II.

S. schottmulleri B (Landsteiner, 1931) Pneumococcus I (Witebsky et al., (10) 1935) B. anthracis (capsule free) (Ivanovics, (11) 1940)	Human blood group "A"
Sh. dysenteriae (Eisler, (12) 1931) Pneumococcus XIV (Finland et al., (13) 1938)	All human blood groups

Morgan (9) isolated from Shiga bacilli an active substance which precipitated an anti-shiga immune serum in dilutions of 1:12,000,000. When this substance was analyzed, it proved to be a polysaccharide which contained 92% hydrolysable reducing substances and 1.6% amino-N. It was found to react with anti-sheep serum as well as with anti-shiga serum.

Of great interest are the inter-relationships which exist between certain bacteria and human blood groups (table II). Some of them react with one of the blood group substances only, while others do so with all blood groups.

In this connection it may be worthwhile to point out that the polysaccharide of those Pneumococci which are known to be nitrogen free (II and III), are heterogenetically inert, while those which contain approximately 5% nitrogen (I and XIV) and resemble human "A" substance more closely, are heterogenetically active.

At the present time there is known a long list of serological inter-relationships between micro-organisms (table III), all of which seem to depend on active polysaccharides.

Some of these bacterial polysaccharides are nitrogen free, others are nitrogen containing substances; however, only a few of these compounds have been studied in sufficient detail to approach their chemical constitution.

All three groups of polysaccharides discussed so far may be subjected to the following general considerations: It is not inconceivable that by extracting the heterophile antigens from their cellular environment, some undesirable breakdown of the active principle might occur. The only guiding indication we have as to the mildness of our procedure is the maintenance of serological activity. However, it is well known that this activity does not necessarily have to depend on the entire complex molecule since haptenes may retain their effectiveness in vitro. A possible example of this sort is given in the somewhat controversial findings of Boivin and Mes-

TABLE III.

Pneumococcus I	B. coli (capsulated)	Barnes et al., (14) 1935
Pneumococcus II	B. friedlanderi B	Avery et al., (15) 1925
"	Saccharomyces cerevisiae	Sugg. et al., (16) 1929
"	B. lactis aerogenes	Julianelle (17)
Pneumococcus XIV	B. anthracis (capsule free)	Ivanovics (11) 1940
B. friedlanderi C	B. rhinoscleromatis	Small et al., (18) 1932
Meningococcus	B. anthracis	Zozaya, (19) 1931
"	B. mesentericus	" " "
"	B. subtilis	" " "
"	Proteus vulgaris	" " "

robeanu (20), and Partridge and Morgan (21). The first mentioned investigators extracted the Shiga organisms with trichloracetic acid and obtained a toxic substance which yielded on mild acid hydrolysis, a non-toxic polysaccharide, a lipoid and fatty acids. From this they concluded that the original compound is most likely a glycolipoid combination. The other investigators extracted the same organism with diethyleneglycol and dissociated the product with formamide obtaining a phospholipid, a polysaccharide, and a polypeptid. Since in this latter preparation the lipoid played only an insignificant role, they concluded that the polysaccharide-polypeptid complex, rather than the lipoid combination, was the important one and constitutes the complete antigen. They also demonstrated that by injecting this complex into rabbits, not only anti-shiga agglutinins but also anti-sheep agglutinins were formed. In 1943 Morgan went even a step further: He injected a mixture of the purified "A" polysaccharide from peptone and the peptide moiety from the Shiga organism into rabbits and succeeded thereby to produce anti-"A" substances. In face of this evidence, Morgan seems to have proven his contention that at least in the case of the Shiga bacilli the heterophile antigen is a polysaccharide-peptide complex and not a polysaccharide-lipoid combination.

In conclusion it may be interesting to point out that type specificity and heterophile behavior are both linked to polysaccharides, while species specificity is definitely related to proteins only.

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EFFECT OF DERMATITIS HERPETIFORMIS ON AUTOGENOUS TRANSPLANT

ALFRED B. FALK, M.D.,* and RALPH GRADMAN, M.D. F.A.C.S.*

ASIDE from the surgical aspects of indications and technic of performing a transplant of the skin, there is little mention in the literature of the course of grafted skin in a systemic dermatological disorder. The following is such a situation in a patient having Dermatitis Herpetiformis. A Thiersch graft from an apparently normal donor site assumed the pathological features of the recipient site.

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Report of a Case

A.M., a 42-year-old white male, complained of an eruption present on the face, forearms, sacral area and posterior surface of the left leg. The lesions recurred intermittantly for 6 months.

Physical examination revealed grouping of vesicles in the above areas associated with a

moderate degree of pigmentation and pruritus. Laboratory study included examination of a section of the skin from the right arm. Vesicles were present between the epidermis and cutis which contained fluid and some round cells. The blood and differential counts were within normal limits.

A diagnosis of Dermatitis Herpetiformis (1) was made and the patient observed for eight months. Treatment with sulfapyridine in doses of two to three grams a day gave marked improvement whereas elimination of the drug resulted in an exacerbation of the disease.

In September 1947, the patient received a sharply localized injury to the upper third of the posterior surface of the left thigh traumatizing a small zone of vesicle-bearing skin. The area failed to heal and soon took on the characteristics of a typical Meleney (2) ulcer. The ulcer measured 10x8 cm. and had a central necrotic plug with an undermined periphery which extended through the subcutaneous fat layer exposing the dense deep fascial tissue. Cultures from the ulcer revealed the presence of microaerophilic non-hemolytic streptococci and hemolytic staphylococcus aureus.

The initial treatment of the ulcer consisted of debridement of the necrotic areas followed by the application of activated zinc peroxide (3) locally, and aqueous solutions of Penicillin intramuscularly. The latter was administered in doses of 40,000 units every three hours for several weeks. No sulfapyridine was given at this time and no vesicles reappeared. Since the ulcer did not respond to the above therapy after two weeks, surgical management was instituted without further delay.

Wide excision of the diseased undermined ulcer edges was performed under regional field block anesthesia using 40 c.c. of 1% Novocaine. A three-quarter split thickness graft was removed from the anterior aspect of the same thigh. This area was never involved as a site of the vesicles of Dermatitis Herpetiformis and appeared perfectly normal at the time the graft was taken. The graft was held in place over the debrided ulcer area with fine mesh vaseline gauze pressure dressings. No sutures were used. Both donor and recipient sites healed uneventfully.

Following the patient's release from the hospital, he was perfectly well for a period of three weeks. No medication was taken at this time. He then developed a typical and severe exacerbation of the Dermatitis Herpetiformis. There was reactivation of all the original sites of involvment including the area recently covered by the autogenous skin graft. The donor site of the graft was not involved.

The patient was immediately put on sulfapyridine therapy with speedy remission of all active sites, including the vesicles in the graft.

Discussion

We know little of the pathogenesis of Dermatitis Herpetiformis. It is agreed that pressure areas are more prone to develop groups of vesicles than locations free from trauma. Using skin with a latent tendency to form vesicles, in a site exposed to irritation, may account for the change in character of the graft .

Summary

1. A patient with Dermatitis Herpetiformis developed a typical Meleney ulcer.

2. A split thickness graft assumed the pathological characteristics of the tissue it replaced.

3. The donor site never showed lesions of Dermatitis Herpetiformis.

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PROPERTIES OF CANCER CELLS*

E. V. Cowdry, Ph.D.**

THIS paper is a summary of investigations by the Barnard Hospital group during the past ten years. We are attempting to discover how cancer develops in previously normal mouse epidermis in consequence of repeated cutaneous applications of 0.6% methylcholanthrene in benzene. I am speaking for the whole group of workers, to whom credit has been given in previous papers of which the most recent was in the J. Am. Med. Assoc. 1947, **146:** 408-411.

After measuring a few properties of epidermis at intervals in carcinogenesis it was observed that some properties remain constant while others change. Both are, of course, of equal interest to us in our efforts to ascertain the conditions of cell life in epidermis reacting directly or indirectly to the carcinogen. The qualification "directly or indirectly" is essential because the carcinogen does not persist as such long after each application. Its place is taken by other fluorescent compounds which likewise disappear, and the cellular population continuously is being replaced. The relation of the carcinogen, and/or its products, to the few cells that actually become malignant, will be a difficult matter to determine. We hope by incorporation of radioactive carbon in the methylcholanthrene molecule to trace the association, if any, between the carcinogen and cell fractions from epidermis treated with it. But the only progress made thus far has been the successful collection **en masse** of pure nuclear chromatin threads, and other cellular components each separately by differential centrifugation.

An interesting phenomenon was repeatedly noted in the reacting epidermis, which we believe to be significant. It is that the alterations appear with few exceptions promptly, usually in the first five days, or earlier, and persist with remarkable constancy to the time of appearance of the cancers when study of the epidermis is discontinued since the scene then shifts to cancer. In fact, it is clear that a new kind of chemical equilibrium is established in many, but not in all, properties of epidermis which is hyperplastic, and precancerous in the sense that the stage is set somewhere in it for the malignant change to take place. Details are given in various publications. Suffice it here merely to list the properties, which, compared with those of normal untreated epidermis show no change, are increased or decreased slightly, or over 50 percent.

Properties of Precancerous Hyperplastic Epidermis Compared with those of Normal Epidermis

INCREASE: (50% or more)	Cell and nuclear volumes, mitotic frequency, cytochrome oxidase (in late hyperplasia), arginase (in early hyperplasia).
INCREASE: (less than 50%)	Abnormal mitoses, magnesium N P ratio, choline, inositol, pyridoxine, water content, arginine, cystine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, valine.
NO CHANGE:	Ascorbic acid N P ratio, specific activity of P 32 in phospholipid fraction, potassium N P ratio, sodium N P ratio, free to bound calcium ratio, p-aminobenzoic acid, succinic dehydrogenase, cytochrome c, adenylpyrophosphatase, histidine, tryptophane, ammonia (in late hyperplasia), arginase (in late hyperplasia), calcium^{45} uptake and retention (in early hyperplasia).
DECREASE: (less than 50%)	Nucleocytoplasmic ratio, cholesterol P N ratio, lipid phosphorus dry wt. ratio, copper N P ratio, zinc N P ratio, desoxyribonucleic acid wet wt. basis, urea wet wt. basis, ammonia (in early hyperplasia) wet wt. basis, calcium^{45} uptake and retention (in late hyperplasia).
DECREASE: (50% or more)	Total lipid P N ratio, calcium N P ratio, iron N P ratio, biotin

N P—nitrogen phosphorus
P N—protein nitrogen

Opinions will differ as to the interpretation of these changes, and absence of changes, in the properties. However, it is safe to say that the conditions of life in the cellular population as a whole have been fundamentally changed. The cells must face deprivations and hardships to

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* Lecture delivered at The Chicago Medical School Seminar, May 5, 1948.

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which epidermal cells are not normally subjected. As is to be anticipated in making the necessary adjustments, the cells change. They swell and become larger both in cytoplasmic and nuclear volume, but the nucleocytoplasmic ratio declines. Cell division is speeded up in frequency and the nuclei show distinctive changes — decrease in thymonucleic acid, increase in displaceability of chromatin and nucleoli by ultracentrifugal force, and abnormal mitoses. In the chromosomes themselves, there is a decrease in desoxyribonucleic acid.

The principal handicap seems to be felt more by the spinous cells than by the basal ones. Their increase in size is greater and the displaceability of their nuclear contents is more marked. Demineralization, revealed by the microincineration technique, is often greater in the intermediate epidermal zone occupied by spinous cells than in the more distal and more proximal zones. This may signify that the spinous cells suffer more from calcium (the chief component of the predominant white ash), and perhaps from other deficiencies, than do the basal cells nearer the source of supply in the underlying dermis. The normal epidermis of the backs of mice is so thin that a clearcut distinction between spinous and basal cells is not obtained, but in the normally thick epidermis of their foot pads this distinction is marked, and mitotic frequency is greatest in the spinous cells. We attach some significance to the fact that in precancerous hyperplastic epidermis maximum mitotic frequency is in the basal layer. It is as if conditions for cell division were unfavorable in the spinous layer as compared with the better located basal layer. Moreover, in the spinous cells, abnormal mitoses are more conspicuous than in the basal ones.

Purely as a working hypothesis, we entertain the idea that the malignant change is a mutation in a small number among the legion of spinous cells subjected to the brunt of the deprivations. In terms of Spencer's theory, it is a rare event in a struggle for existence, which, in this case, has gone on for a long time.

We come now to the actual cancers. The properties of these have been measured by the same techniques. But it was not feasible to work with each cancer as it develops in the precancerous hyperplastic epidermis. Resort is made to analysis of pooled transplants of a single cancer, now in the 56th generation and growing with great regularity. Only small transplants with minimum necrosis and of uniform size are taken. Allowance is made for about 4 percent by weight of blood. The changes, and the absence of changes, from the conditions that characterize the chemical equilibrium of the precancerous hyperplastic epidermis are summarized in the same way.

Properties of Squamous Cell Cancer compared with those of Precancerous Hyperplastic Epidermis

INCREASE: (50% or more)	Lipid phosphorus dry wt. ratio, choline, inositol, succinic dehydrogenase, adenylpyrophosphatase, arginase.
INCREASE: (less than 50%)	Abnormal mitoses, p-aminobenzoic acid, pyridoxine, biotin, water content, isoleucine, leucine, lysine, methionine, tryptophane, threonine, valine.
NO CHANGE:	Ascorbic acid N P ratio, specific gravity of P 32 in phospholipid fraction, histidine, phenylalanine.
DECREASE: (less than 50%)	Potassium N P ratio, sodium N P ratio, magnesium N P ratio, iron N P ratio, cytochrome oxidase, desoxyribonucleic acid dry wt. basis, cytochrome c, arginine, cystine, calcium^{45} uptake and retention, free calcium.
DECREASE: (50% or more)	Calcium N P ratio, iron N P ratio, copper N P ratio, zinc N P ratio, urea wet wt. basis, ammonia wet wt. basis.

N P—nitrogen phosphorus
P N—protein nitrogen

At least it is clear that, in these cancers conditions of cell life are different from those given in the first summary for hyperplastic precancerous epidermis. This does not necessarily mean that carcinogenesis is a process involving two alterations: **first,** that from normal to what we call precancerous, and **second,** that from precancerous to cancer. The chemical changes from normal noted in the first summary are derived from analyses of the reacting epidermises from several mice pooled to supply sufficient volumes of tissue. The range in variation of properties, locally in a single epidermis, and between epidermises of different mice, is not known. The malignant transformation is usually confined to a few cells in a single location within a relatively

enormous cellular population. In their manner of life it is possible that these few cells resemble those of the cancers more closely than do those of the hyperplastic epidermis as a whole. Because their volume is so tiny, compared with that of epidermis actually not precancerous, we could hardly expect their properties to be revealed by analysis of whole epidermis. Therefore, the cancerous chemical equilibrium may not be altogether lacking in such small foci located, as they are, in relatively so very large stretches of hyperplastic epidermis. It will be a long time before this question can be answered for it will be necessary first to devise and to use quantitative analytical techniques applicable to areas of epidermis of microscopic dimensions. The possibility is an important one, not to be ignored, that some cells may have undergone the malignant transformation and do not display it because they are still immobilized within the hyperplastic epidermis.

From these two summaries some features in the transition from normal epidermis to cancer can easily be calculated. Thus the decrease in the calcium N P ratio is about 75 percent being in the cancer of over 50 percent from the decreased amount present in the precancerous hyperplastic epidermis. The marked decrease in biotin in the hyperplastic epidermis is to some extent compensated for by a lesser increase in the cancers as compared with the conditions of affairs in the hyperplastic epidermis. The slight increase in water content in hyperplastic epidermis is accentuated by a further increase in the cancers. Arginase activity increases in early hyperplasia but subsiding to normal in late hyperplasia only to increase greatly in the cancers, and so on.

We are particularly interested in the calcium deficiency. It is not only an absolute decrease in total calcium but also in the proportion of free to nondiffusible calcium. That is, free calcium is most decreased and the uptake of calcium^{45} is decreased so that the cancers show an inability to take in calcium. Investigators have found that in other tissues decrease in free calcium loosens the intercellular material so that the cells fall apart. Perhaps the anchorage of the epidermal cells in the precancerous stage fails with a decrease in free calcium that may occur in a small area and pass unnoticed in the determintions of whole precancerous epidermises. At any rate, the invasiveness of growing cancers may be correlated with the undoubted decrease in free calcium.

In addition to a possible breaking down of the cohesiveness of the epidermal cells by the calcium deficiency a spreading factor may facilitate invasion. Simpson and Gopal reported at the recent meeting of the American Association for Cancer Research in Chicago that injections of hyaluronidase in the immediate vicinity of the cancer transplants promotes metastasis.

The nondiffusible calcium is probably bound to protein. Evidence of alterations in the amounts of some amino acids, are therefore important. The decreases in urea and ammonia also suggest a modification in nitrogen metabolism. Changes in the activity of enzymes loom large in even a sketchy formulation of the distinctive manner of life of the cancer cells.

It is hardly necessary to say that only a beginning has been made in the measurement of properties of epidermis in this carcinogenic series. Other properties will be studies as we can find or devise techniques for their accurate measurement. In the broad view, the project involves research at 4 levels in both mice and humans.

The **first** is the fact-finding investigation of properties of epidermis in the precancerous state, that is, in the hyperplastic condition antedating the local appearance of cancer. Some data on mice have been given. Our purpose is to concentrate on senile keratotic lesions in humans.

The **second** is the experimental search with these properties as clues for means whereby the development of cancer can be inhibited even though the precancerous stage has been set for its appearance. This is chemotherapeutic in nature and it is likewise easier to work with mice than with humans.

The **third,** like the first fact-finding stage, to discover the distinctive properties of the cancers in mice. A few data have been presented in the second summary. In human squamous cell cancers of epidermal origin there is a similar calcium deficiency .

The **fourth** level is again the experimental search with these properties as clues for means of overcoming the malignant features of cancer

cells or of selectively killing them. Mice are for us the proving grounds of techniques to be extended, of course, to the human cancers. In conclusion I think it is interesting to compare the "final common path" of our physiological friends with carcinogenesis.

Final Common Path	Carcinogenesis
Stimuli are of wide variety.	Carcinogens also of wide variety.
Some are essential for life.	Some are essential for life.
No common property is exhibited by all stimuli.	Carcinogens have no common property.
Hypersensitivity to stimuli can be induced.	Susceptibility to some carcinogens can be induced.
Different stimuli can produce similar motor responses.	Different carcinogens can produce similar cancers.
Stimulus only initiates impulses, then fades out.	Most carcinogens only initiate chemical events, then fade out.
Impulses pass through neurones in sequence.	Chemical events may well occur in sequence.
In passage resistance at synapses is overcome.	Resistance may have to be overcome in replacing one chemical cellular environment by another.
Passage through persistent, definitely localized channels.	Each chemical environment wipes out preceding one in same area.
Little time is lost.	Much time is lost.
Impulse may not reach through final common path and excite muscle.	Sequence in cellular chemical environments may not culminate in one favoring a malignant transformation.
Impulse can be strengthened by impulses resultng from other stimuli.	Sequence can be strengthened by other chemical events resulting from other carcinogens.
Impulse can be inhibited by cortical control.	Sequence, when weak, can be inhibited by caloric destruction.
Final chemical kick delivered to muscle may be the same.	Final change effected in cells may be a mutation.

To prevent cancer by avoiding carcinogens is almost as impracticable as to live without stimuli. It must be admitted that different carcinogens can produce similar cancers as well as different stimuli similar motor responses, and that in the case of both we have to reckon with stakes of hypersensitivity. The carcinogens initiate a sequence of chemical events as the stimuli do and both sequences may fade out not reaching the end result of cancer or muscular contraction. Inhibiting and accelerating factors operate in both. We must discover what these are and attempt to prevent precancerous lesions from progressing to cancer. The early cancers are of microscopic size and may forever escape detection **in vivo.** The chief hope is to correct the askewness of cancer cells which we have stressed or to discover their weaknesses and to incapacitate or kill them selectively. It is an inspiring job.

OBTAINING MEDICAL HISTORIES BY INDIRECT QUESTIONING

H. H. GARNER, M.D.*

THE importance of an adequate medical history is stressed in medical school teaching and its value as a diagnostic procedure for the externe and the interne is not to be minimized. An adequate history is essential to good medical and surgical diagnosis; however, it is felt that insufficient attention has been given to the suggestive influence of "history-taking." During a period of over four and a half years of military service, I was especially impressed by the possible suggestive influence in the taking of a history and the deleterious effects of frequent examinations in suggesting disability to the patient. There were several reasons why histories taken in the conventional fashion, described as desirable in the medical school, were suggestive in the military service.

1. The goal of the soldier is frequently illness rather than good health.
2. Examinations are repetitive.
3. Examinations may be limited in scope, suggesting the sphere of important observation for the physician.
4. The soldier may be evacuated through several echelons and on more than one occasion through the same echelons; he will thereby attach special significance to the questions which will have been repeated.

History-taking by the usual accepted method, was modified to meet the problems outlined above, and was found to be very desirable in military service. I have found that the problem in civilian practice contains essentially the same discordant elements and that similar changes would be desirable in civilian practice.

The chief complaint can be elicited by using commonly accepted questions as to the reason for seeking medical aid. One often finds that the present complaint is elicited by a question such as, "What is wrong with you?" Although a suggestive question, it is a reasonably innocuous one, so that it cannot be strongly criticized. We prefer, however, such questions as, "What is the reason for your being in the hospital?", "Give me an idea of what was troubling you which led to your seeing the doctor?", etc. The patient is then allowed to give the chief complaints with little further interruption. Such questions as, "Is there anything further you can tell me about that symptom?", aid in expanding the information with regard to the chief complaint.

The family and personal history as usually elicited is not likely to be "symptom producing". A warning note is offered in that the manner of questioning and the questions as put to the patient may have an influence on his attitude toward his illness.

The present illness is elicited by asking the patient the when, where and how of the illness. "Tell me when you first observed your trouble?", "How did it begin?", "Where did it affect you most?" "What happened next?", "Did you notice anything else?", are questions which may be used to elicit and expand on the onset and course. Good listening ability and restraint in giving leading or suggestive questions are necessary.

The greatest source of suggestive "symptom giving" arises in that part of the history which has been referred to as the inventory of symptoms. It is here that the physician, as a result of previous training, is likely to err in voicing a set of symptoms in a manner so suggestive as to create symptoms previously not available to the patient. The number of suggestive symptoms which can be offered to the patient are too many to mention; not only are they questions used once, but if a patient is seen by several physicians, they may be used on several occasions, so that by the time the patient has reached the hospital the whole symptom complex has become thoroughly fixed in his mind.

A clearer concept of what is being stressed will be obtained by observing the manner in which an organ system examination is frequently made, and how a similar history can be elicited without any emphasis on suggestive symptoms.

A patient admitted to a clinic for a possible eye injury associated with blepharospasm was

(Continued on page 22)

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CLASS OF 1948

On June 26, 1948, commencement exercises were held at the First Methodist Church in the Chicago Temple Building for the Class of 1948 of The Chicago Medical School.

Following the invocation by the Rev. John C. Evans, an unusually challenging address was delivered by Dr. Bernard Iddings Bell of the University of Chicago. Dr. Bell remarked that it was his experience that graduates were interested mainly in insuring the fact that they would make a success of their lives. While agreeing that it was a worthy ambition in any individual, Dr. Bell argued that, in his opinion, it was far more important for one to prepare

The CHICAGO MEDICAL SCHOOL

himself not for success, but for failure, for it was only that person who can withstand the adversities of fate and the disappointments which life visits upon us all, who can, in the end, find peace and happiness in his life.

Following the commencement address the candidates for the Degree of Bachelor of Medicine were presented by Dr. John J. Sheinin, Dean of The Chicago Medical School, and the degrees were conferred by the Rev. John C. Evans, Vice Chairman of the Board of Trustees, who then delivered a statement concerning the progress of The Chicago Medical School during the past year and its hopes and aims for the future.

MEDICAL HISTORIES —

(Continued from page 19)

confronted with such questions as, "What happened to your eye?", "Can you open your eyes?", "Can you see ", "Does it hurt?". All of the foregoing questions suggest that the patient actually sustained an injury to the eye, that he is unable to open his eyelids, and that he cannot see. These are reinforcing questions and suggestions which tend to produce the idea that a serious disability exists. An approach, in which reassurance and suggestion by emphasis may convert the patient from one with a disability requiring hospitalization to one who can be immediately "cured," is desirable. The following technique would be more desirable. After an appraisal of the situation, the patient is told in a positive and reassuring manner: "Open your eyes." An examination is made of the eyeball to assure the examiner that no serious injury exists. The patient is then asked: "What happened to you?" Such questions as may elicit further information about the patient's ocular symptoms may then be used: "What did you notice?", "How were you affected?", "Did you notice any other symptoms?", etc. Another example of "history-taking" by the indirect method may more clearly demonstrate the possibilities of direct and indirect questioning. A typical example of a history being taken by a medical student or interne after the initial complaint and the history of the present illness had been elicited might proceed as follows: "Where do you have the pain?", "How long have you had the pain?", "Do you vomit?", "Did you ever vomit before?", "Did you ever notice blood in your stools?" It is not uncommon to hear a series of the above and similar questions given to a patient complaining of epigastric pain or discomfort. We have found that a good history can be obtained through indirect questioning with such questions as: "Describe your discomfort?", "When do you notice it?", "Where do you notice it?", "Have you noticed anything else about your condition?", "What about your eating and appetite?", and if the patient indicates that he has vomited: "What did you notice about your vomiting?", "What was in the stuff you vomited?", "Have you noticed anything about your stool?", "Did you notice anything in your stools?". We have found that an adequate medical history can be obtained by using such indirect questions. The possibility of improving and increasing the available information through further direct questioning exists. The end result is a very adequate history without "giving" the patient any symptoms. The above examples indicate the possibilities involved in "history-taking" by the indirect method. The same method may be applied with equal success to any organ system.

SUMMARY AND CONCLUSION. It would seem desirable that a revision in the commonly accepted instruction for medical "history-taking" be considered. Since the goal of the patient is frequently ill health rather than recovery, he is very susceptible to the influence of direct "history-taking", which is associated with the "giving" of symptoms for a Yes or No response. Since some concept of a relationship of the various symptoms suggested in the interview with those that he has is already present in the patient's mind, he readily weaves his previously recognized symptoms with those offered in questioning. Repeated questioning along similar lines from echelon to echelon of the medical service further accentuates the significance of the symptoms to the patient. A good history can be obtained by indirect questioning and this type of "history-taking" would seem most desirable in medical practice.

PRE-PARTUM HEMORRHAGE

STANLEY REICHMAN*

IN THE early years of this century, when less scientific obstetrics was the rule and the home practitioner reigned, the three most common complications encountered in the pre-natal period were infections, the toxemias of pregnancy and hemorrhage. But with the recent advent of antibiotics, and with the detailed care exercised by the modern obstetrician during the nine months of pregnancy the dread of the two former has been greatly alleviated. However, hemorrhage still ranks as a prime cause for maternal death and fetal mortality, and in some cases may be a direct result of interference on the part of the physician. It is well, therefore, for the physician to have a complete understanding of the factors producing pre-partum bleeding, and even clinically more important, for him to be able to recognize the condition at hand and adequately treat it. It will be the scope of this paper to briefly review the recent literature on the diagnosis and treatment of the most common causes of hemorrhage during the pre-natal period. The conditions will be divided among the trimesters of pregnancy and each discussed under the heading of the period in which it most commonly occurs. It will not be attempted, however, to completely cover every possible type of bleeding occurring from the onset of fertilization and implantation up to actual parturition. Rather, only the more important and commoner conditions will be discussed. In the first trimester abortions and ectopic pregnancy are the most frequent complications. During the second three months hydatidiform mole is often seen, and during the last third placenta previa and premature separation are most common. During any of the trimesters extrinsic causes of bleeding may be seen; and therefore it is perhaps well to begin with the latter.

Extrinsic Causes of Bleeding (1)

The diagnosis of lesions of the cervix, of the vagina, or of the vulva is usually made upon finding the lesion. The only real exception to this is seen in cases of vaginal or vulval varices, in which cases there may be diffuse bleeding. The treatment depends upon the lesion and is usually specific.

It must be mentioned at this point and stressed to the utmost that cases of intermittent spotting must be thoroughly investigated, for there is no reason why a pregnant woman may not develop carcinoma of the cervix. If there is the slightest question as to the presence of such a lesion (for ulcerations and erosions may make gross diagnosis difficult), a biopsy must be taken. The life of the woman may depend upon this, for it can readily be seen how the pounding of actual labor may result in the rapid metastasis of early growing cancer.

First Trimester

Spontaneous abortions are probably the most frequent cause for the inability of the woman to reach term, in addition to being the commonest cause of bleeding during pregnancy. It is, of course, to be differentiated from the induced abortion which may be either criminal or therapeutic.

The condition is defined as the extrusion of the contents of the uterus before viability. It may be incomplete if the placenta or membranes or both are retained, or complete if they are not. Systemic causes such as diabetes, thyrotoxicosis, organic heart disease, blood dyscrasias and incompatible Rh may be responsible and must be eliminated or as adequately treated as possible. Maternal factors such as infection fibroids, and malposition may be more difficult to treat per se, but today, the greatest emphasis is placed on the endocrine management.

It is perhaps well to first review the normal endocrinology concerned with the maintenance of the gestation period, for it is upon these concepts that modern therapy is based (2).

Following nidation, the ruptured follicle undergoes changes and becomes known as the corpus luteum of pregnancy. It produces, under the direct influence of prolan B, the gonadotropic substance elaborated by the pituitary, a hormone known as progesterone. The latter, in turn, produces endometrial changes favorable for growth, nidation and development, and inhibition of uterine contractions. In addition, the corpus luteum also plays a part in the production of

*M.B., 1948. The Chicago Medical School.

the estrogenic hormone which has primed the uterus for the action of progesterone. Hamblen (3) suggests that unless estrogen and progesterone are present in the proper portions, inhibition and normal quiescence of the uterus will not be maintained. Proper functioning of the corpus luteum is thus an absolute necessity during the first trimester. Actually, however, its action soon begins to fade, and though the amount of progesterone and estrogen produced from it wanes, it is directly replaced by the syncytial cells of the chorioepithelial system (2). By the fourth month, the latter takes over completely.

Thus it is recognized that three phases of endocrine deficiency may exist: 1) in the immediate post-ovulatory state, in which deficiencies in the gonadotropic hormone or abnormalities of the ovary may result in insufficiency of the corpus luteum; 2) in later inadequacies of the corpus luteum, for the same reasons; and 3) in inadequacies of the placental production. It is interesting at this point to note that the incidence of complete abortions in cases of deficiencies have a direct effect on the future pregnancies which are affected for the same reasons. Malpas, (4) in a study of 6,000 abortions, found that if a woman had had one abortion previously she had a 78% chance of not repeating it . With two previous consecutive abortions, she had a 62% chance of not repeating it; with three, 27%; and with four, 6%.

There are three currently discussed types of abortions:

1) **the threatened**—usually in the first trimester. There is some spotting with mild uterine cramps (significant of attempted early expulsion of the uterine contents). The cervix is usually closed.

2) **the imminent**—may procede further with increase to continuous bleeding and cramps. The cervix is soft and patulous and usually admits the fingertip.

3) **the inevitable**—bleeding is profuse with distinct labor pains. Examination frequently reveals a piece of placenta or fetus in the cervical canal. Diagnosis usually depends upon a history and early presumptive and probable signs of pregnancy, with onset of bleeding, cramps, and pelvic findings. Most important to differentiate is ectopic pregnancy as described below.

Once the diagnosis has been made, it is important that proper therapy be instituted. Hudson et al., (6) in a series of 1,000 consecutive pregnancies in which 94 spontaneous abortions were seen of which 68 were threatened, state that treatment with bed rest and progesterone produced recovery in 43%. However, because of the effect of estrogens many feel that progesterone replacement by itself is insufficient. Hamblen (7) claims that both are indicated and advocates the use of 3.75-7.5 mg. premarin and 30-60 mg. of pranone. In a series of 24 cases, Voux and Rakoff (2) advocate similar doses using different products. Ten mg. of progesterone proluton* and 10,000 rat units of alpha-estradiol benzoate as progynon B*, two to three times weekly in the same syringe. Fifteen of the 24 cases (between the ages of 21-36) went to full term without complications. There were three prematures. Thus it is seen that the percentage of good results in this series is higher than that seen in the series with the use of progesterone alone.

In addition, it must be noted that bed rest, sedation, ice bag to the abdomen, vitamin K, soft diet and no enemas are all indicated. Some men also advocate the use of Vitamin E as well as thyroid extract gr. ½ BID.

Ectopic Pregnancy (1), (5) is defined as any pregnancy outside the uterine cavity, commonly in the tube, but even in the ovary or abdominal cavity. The condition, because of its marked variability in symptomatology, may be difficult to diagnose. Classically, there is a history of pregnancy with sudden onset of severe pain in either quadrant radiating to the rectum, followed by collapse with a picture of shock. A chemical peritonitis may be present, but because of the variable manner in which the rupture may occur (8) the picture may not be clear cut. Immediate surgery is indicated if the diagnosis is certain, and exploratory may even be necessary in doubtful cases. Posterior colpotomy with aspiration of bloody fluid may be of aid in the diagnosis.

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* Schering

Second Trimester

Hydatidiform Mole (5). Atypical uterine hemorrhages are seen with this vesicular degeneration of the chorion in which proliferation and degeneration of the stroma of the villi and increase of the syncytium are manifest. Abdominal pain, nausea, vomiting, and absence of fetal movements are seen as well as signs of toxemia. The diagnosis is aided by rapid growth and globularity of the uterus, absence of fetal body on palpation and x-ray, strongly positive A-Z test and the general evidences of illness. The treatment consists of complete emptying of the uterine contents.

Third Trimester

It is easily emphasized that hemorrhages occurring from the eighth month to term are of serious consequence if not properly cared for, since at this time the uterine contents are more liable to be viably delivered and improper management of the bleeding may result in severe deleterious effects not only to the mother but also to the baby.

To be differentiated at this time are premature separation of the placenta, placenta previa, and those cases of excessive bloody show in which careful examinations of the placenta after normal full term delivery reveals no evidence of previa, accidental bleeding or any other pathology.

Placenta Previa. This condition, defined (5) as the development of the placenta in part or in its entirety within the zone of dilatation of the cervix, should be suspected in any case of painless, bright red bleeding, apparently without cause. It is also known as unavoidable hemorrhage. It is classified as to its location, the central or total type lying directly over the os, and the partial (divided into marginal, and lateral) in which cases only a portion of the placenta lies over the canal. Low implantation of the placenta is not considered by some to be a true previa, but it is mentioned here and classified as a form which may give rise to symptoms of previa.

Diagnosis may be difficult, but in the presence of painless bleeding thorough examination is indicated. Carefully performed vaginal may reveal a palpable central or partial previa. X-ray may help in those non-palpable cases. Montgomery (1) advocates rupture of the membranes and traction on the head when partially dilated or bringing down one leg so that the buttock acts as tamponade against the lower uterine segment, or section if the cervix is closed and the bleeding is severe. Scott (9) more carefully claims that clinical experience and judgment is more important and that after hospitalization the following factors must be considered in each case before treatment is undertaken: site of placenta, amount of hemorrhage, parous condition of the patient, whether or not labor had begun and how it is progressing, duration of pregnancy, presentation, and viability. More radical treatment is advocated in only the complete or total types of previa. Methods used include medical induction, spontaneous labor following artificial rupture of the membranes, vaginal packing, use of a metreurynter, version either internal or external, and Cesarian, either Classical, low or Porro.

Premature Separation of the Placenta. Also called abruptio placenta, ablatio placenta, and spoken of as accidental hemorrhage, it is seen in the third trimester, and may be defined as a separation or detachment usually of a portion of the placenta situated low in the uterus just above the lower uterine segment. It is frequently seen in pregnancy toxemia, cardiovascular-renal disease, and trauma, and is characterized by (5), (1) either external bleeding which may be profuse or concealed bleeding, stormy onset, internal or external board-like rigidity of the uterus, constant, severe abdominal pain and tenderness, and possibly associated hypertension or toxemia or history of trauma.

The treatment depends upon the severity of the case and here again good judgment and clinical experience play a major role. Montgomery (1) suggests rapid delivery if possible or abdominal Cesarian if the cervix is closed. Scott et al. (9) advocates section only in two extremes: when the baby is alive and labor has not started or in cases of severe uterine apoplexy with hemorrhage into the uterine wall (Couvelaire uterus). Even in the latter cases conservative therapy is sometimes recommended. In all events blood loss must be replaced and impending shock treated. Vitamin K may also be used. Lastly, it can readily be seen that many difficulties may be

(Continued on page 38)

Abstracts

SOME TOXIC EFFECTS OF ACID AND NEUTRALIZED THIAMINE SOLUTIONS. Jay A. Smith (by invitation), Piero P. Foa, Harriet R. Weinstein (by invitation), A. Sidney Ludwig (by invitation), and J. Marvin Wertheim (by invitation). Department of Physiology and Pharmacology, The Chicago Medical School. Federation Proceedings, Vol. 7, No. 1, March, 1948.

Thiamine hydrochloride solutions are acid. Upon injecting such solutions intravenously, respiration is depressed, and blood pressure decreases; these effects are transitory if artificial respiration is provided. It was desired to know if these changes were due to the thiamine or to the acidity of the solution. Thiamine hydrochloride solutions weakened or stopped the isolated perfused turtle heart; neutralized solutions depressed the heart slightly; acidified Ringer depressed the heart less than a thiamine solution at identical pH. Thiamine hydrochloride solutions caused vasodilation in the perfused rabbit ear in proportion to the concentration and the acidity. Neutralized thiamine solutions caused little change in the rate of perfusion. Thiamine hydrochloride depressed the heart in the heart-lung preparations only in concentrations sufficiently great to alter the pH of the blood appreciably. A thiamine hydrochloride solution (pH 3) intravenously to dogs altered the pH of the blood only slightly (from 7.54 to 7.52) within 20 seconds. The injection of identical quantities of a neutralized thiamine solution caused no shift in the pH. The effects on respiration and blood pressure were identical after injection of acid or neutralized thiamine solutions. It is concluded that in isolated systems, such as the turtle heart, rabbit ear, and heart-lung preparation, the effects of thiamine hydrochloride are due principally, although not exclusively, to the acidity of the solutions. In intact dogs, on the other hand, the effects of thiamine are not due to the acidity of the solutions but to thiamine itself.

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LOW SERUM POTASSIUM LEVEL DURING RECOVERY FROM DIABETIC COMA. M. Frankel, M.D., J. Gruen, M.D., and A. F. Willibrands, Ph.D. Arch. Int. Medicine 80, 728-738, Dec. 1947.

During treatment of a patient in severe diabetic coma with large quantities of insulin, water, dextrose, sodium chloride, and sodium bicarbonate, the authors observed a syndrome of muscular weakness, gasping type of respiration due to paralysis of the lower respiratory tract, irregular corrigans pulse, large pulse pressure, dilation of heart, systolic murmurs and high venous pressure. Abnormalities of the electrocardiogram were also noted.

This syndrome manifested itself after the blood sugar and blood bicarbonate levels had returned to normal. It was found that serum potassium content which had been normal on patient's admission to hospital had fallen to 69 mg%. The conclusion reached was that the low potassium was due to the loss during the period of acidosis, a low potassium intake for several days and a shift of potassium from extra to intracellular fluid under the influence of large doses of insulin.

By the use of KCl intravenously, the patient responded quickly and came out of her respiratory difficulty.

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DIABETIC ACIDOSIS. Effect of Administration of Sodium Phosphate. Maurice Franks, M.D., Robert F. Berris, M.D., Nathan O. Kaplan, Ph.D., and Gordon B. Myers, M.D. Arch. Int. Med. 81, 42-55. January 1948.

It is now well recognized that the phosphate cycle constitutes the mechanism whereby energy resulting from oxidation is rendered available to every cell. A noticeable rise in plasma level and urinary excretion of phosphorus has been found in diabetic acidosis. This apparently causes a significant depletion of phosphorus stores in the body as shown by the response to insulin. The plasma and urinary phosphorus levels fall precipitously and remain subnormal for as long as a week after institution of therapy.

The fact that death may occur in circulatory collapse after abolition of ketosis, restoration of a normal blood sugar level and replacement of apparently adequate amounts of water and sodi-

um chloride raises the question of the clinical importance of deficiency of other elements, not only phosphorous and potassium. One of the objectives of the authors' study was to determine the clinical efficacy of intravenously administered sodium phosphate as an adjuvant to therapy of diabetic acidosis.

A rise in serum inorganic phosphorous and fall in organic phosphorus during diabetic acidosis may be due to lack of insulin — the presence of which is necessary for oxidation. The fall in plasma and urinary inorganic phosphorus levels during therapy is probably due to the resumption of phosphorylation with subsequent reconstitution of organic phosphate compounds of the body.

No acceleration in rate of disappearance of acetonuria was demonstrable after administration of sodium phosphate. No greater rise in CO_2 combining power and superior maintenance of plasma chloride levels are expected because of transfer of phosphate to cells. This transfer leaves sodium free to increase alkaline reserve.

There is a striking improvement of the mental state with use of sodium phosphate. This may be due to the fact that carbohydrate is the preferred if not the sole fuel for the brain. When an increased supply of phosphate is made available to the central nervous system—an increased efficiency of phosphorylations and hence of carbohydrate utilization may result.

The authors also note a statistically significant decrease in fatality rate.

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CAPILLARY PERMEABILITY IN RELATION TO ACUTE ANOXIA AND TO VENOUS OXYGEN SATURATION. J. Henry, M.D., J. Goodman, M.D., J. Meehan, M.D., and R. Frankel, M.D. J. Clinical Investigation 26, 1119-1129. November 1947.

The results of the above authors suggest it is necessary for oxygen tension in the capillary bed of the human arm to drop to values below 15-25 mm of mercury, and an oxygen saturation of 15-25 vol %, before any significant change in permeability of vessels to protein can be expected.

Even during decompensation, the oxygen content in blood from the antecubital vein of cardiac patients, only rarely falls to such values. Nor are such values met in pneumonia except in moribund cases.

Aub and Cunningham have shown that in irreversible traumatic shock the venous oxygen content may fall as low as 3-4 vol %, representing saturations of the order of 15-20%. It is possible that in this condition the venous oxygen tension may be low enough to result in a generalized capillary permeability. It has been noted that following saline therapy in hemorrhagic shock, plasma proteins are carried out of the blood stream with the saline and that this occurs to a greater extent in irreversible shock.

It is possible to develop far higher grades of irreversible anoxia and edema in isolated parts of the body such as limbs, ears, or fingers when circulatory obstruction has taken place. The edema so frequently seen in arterial spasm may be explained in this manner.

The preceding observations indicate that anoxia commences to effect the capillary permeability to the point of significant protein leakage at a very low oxygen tension. It therefore usually requires a combination of one or more of the factors: ischemia, anoxic anoxia, anemic anoxia or a great increase in tissue oxygen consumption.

School And Faculty Notes

STANDARD CLUB DINNER SUCCESSFUL

A dinner given for the purpose of raising funds for The Chicago Medical School, was held May 26 at the Standard Club. Mr. Lester N. Selig, chairman of the Board of Trustees, presided over the dinner, which was addressed by the Hon. Mayor Kennelly, Dr. Andrew C. Ivy, vice-president of the University of Illinois, Rabbi Solomon Goldman, and Dean John J. Sheinin.

A considerable amount of money was raised by the nearly 300 guests attending, in addition to the acquisition of many new friends and supporters of the School.

Department of Physiology and Pharmacology

While Dr. Nice attends the centennial meeting of the Association for the Advancement of Science in Washington, D.C., during the week of September 13-17, the remainder of the Dept. of Physiology and Pharmacology will attend the meeting of The American Physiological Society in Minneapolis, Minn.

At the APS meeting the following papers will be presented:

"Secretion of Insulin in the Dog Studied by Means of the Pancreatic Femoral Anastomosis" by Drs. P. P. Foa, J. A. Smith, and Miss H. R. Weinstein.

"Observations on the Curare-like Actions of Thiamine" by Drs. Foa, Smith, and Miss Weinstein.

"Functions of the Pancreas of Alloxan Diabetic Dogs Studied by Means of Cross Circulation Experiments" by Drs. Foa, Smith, and Miss Weinstein.

Dr. A. H. Ryan published a paper in the March 1948 issue of the **Federation Proceedings** on experimental work on "Sympathetic Reaction in Peptic Ulcer." The study was conducted on 50 subjects, 5 of whom had known peptic ulcers while the remainder were non-ulcer subjects.

Microbiology and Public Health

Dr. George J. Scheff spent the month of July at the University of North Carolina doing research on "The Yeast Phase of Histoplasma Capsulatum." Dr. Scheff also presented a paper entitled "The Role of Potassium as a Cause of Death in Experimental Trypanosomiasis" at a recent meeting of the American Society of Parasitology, and at a seminar of the Department of Bacteriology of the University of Illinois School of Medicine, Dr. Scheff spoke on the "Hematological Response to Various Types of Infectious and Bacteriological Products."

Dr. I. S. Neiman recently spoke on "The Clinical Significance of the Tuberculin Reaction" at the American Hospital.

In the spring quarter of 1948, the Department of Microbiology and Public Health presented an elective in Immunology. Further elective courses in Mycology and Virology will be offered in the near future.

Department of Physiological Chemistry

A Tiselius Electrophoresis Apparatus has been installed in the waiting room of the old clinic. The machine is an invaluable tool for research in the nature of complex colloid systems and in the production of purified proteins, enzymes, and hormones. Demonstrations and lectures on the use of this machine and its applications to medicine are being given to classes in Chemistry by Dr. A. R. Goldfarb of the Chemistry department. The Chicago Medical School is one of the few institutions in the country where such demonstrations and lectures are available to the students.

A paper by Dr. R. G. Roberts and Miss D. Hilker entitled "Spectrophotometric Determination of Ephedrine and an Ephedrine-like Substance which can be Obtained from Autolyzing Adrenal Glands" is to be read at the September meeting of the American Chemical Society at Portland, Oregon.

Department of Anatomy

Dr. E. G. Congdon is working with Miss Gillaspie, formerly associated with the Anatomy Dept. on the almost untouched subject of "Census of

the Visceral Nervous Ganglia of the Human Pharynx."

Dr. Leon H. Strong has been devoting much time to a research project involving the vascular developmental patterns of the brain and spinal cord, and certain short projects concerned with the gross physiology of the tongue, pharynx, and larynx. The vascular investigations are made upon a closely timed series of mammalian embryos, injected with india ink by their living hearts, and cleared by the Spalteholz method. The capillary picture approaches completeness, a necessity for a comprehensive study lacking in material injected by external force. The present stock of embryo numbers more than 200. By examination of the embryo as a whole in a liquid medium, then photographing it, and later sectioning the embryo, a rapid three-division study can be made. This obviates the difficulty encountered in the reconstruction of collapsed capillaries which are impossible to follow accurately in uninjected material. The work thus far has shown that a marked difference in pattern of development exists in the basal and alar plates of the developing neural tube. This may be functional but may well be merely an indication of difference in metabolic rate in the closure of the neural tube dorsally. Anomalies in the definitive pattern of vascularization may be traced to earlier patterns and the time sequence of transfer from embryonic to adult vessels can be followed.

The work on the mechanism of laryngeal pitch in man, has made physically untenable the linear tension theory of pitched control and indicates a fretting system, logarithmically controlled. This study is being extended. Motion picture studies of the movement of the tongue show movements in chewing and in tongue controtions inexplainable by any system of muscle fibers in the literature. The present study of the gross physiology of movement has an objective precision movement in speech and otherwise. Microdissection of the smaller force components of the larger muscle masses is being carried out both in the four-month fetus and in the adult.

NEW FACULTY ADDITIONS

Peter Gaberman, B.S., M.D.

Our new full-time associate professor of Medicine, Dr. Peter Gaberman, has had a long association with The Chicago Medical School. He first joined the faculty of the School in 1933 as an assistant in the Clinical Medicine Department. In 1935 he became an instructor in Clinical Medicine, and was made an associate in that department in 1940. In 1941 Dr. Gaberman became assistant professor of Clinical Medicine. The armed forces interrupted this stage of his career and he served in the second World War from 1942 to 1946.

Dr. Gaberman received his professional training at the University of Illinois College of Medicine, from which he graduated in 1927. He began his association with Cook County Hospital in 1927 as an intern, and is now an attending physician at that institution. A Diplomate of the American Board of Internal Medicine, Dr. Gaberman is a member of the American Medical Association as well as of the Medical Associations of Chicago and Illinois.

Dr. Peter Gaberman

David A. Willis, B.S., M.D.

We welcome Dr. David A. Willis to our Clinical Surgery staff as full-time associate professor.

Dr. Willis is a native of Chicago and has centered most of his professional activities in and around this city. He received his professional education at the University of Illinois, from which he graduated in 1922, and served his internship at Cook County Hospital. In 1924 he returned to the University of Illinois to serve on the staff of the Department of Pathology under Dr. Richard Jaffe. During the second World War, Dr. Willis, a lieutenant-colonel in the Army, was Chief of Surgery at the 17th Field Hospital, Tourney General Hospital, and Madigan General Hospital, stationed in the Pacific theater.

Now an attending surgeon at Mount Sinai Hospital, Dr. Willis is a Fellow of the American College of Surgeons, a Licentiate of the American Board of Surgery, and a member of the honorary research society, Sigma Xi.

Dr. David A. Willis

He has an imposing list of research projects and publications to his credit. They deal with such subjects as:

Capillary Permeability
Effects of X-rays Upon the Kidney
Biological Reaction for Hyperthyroidism
Reduction of Fractures Under Local Anesthesia
Effect of Electric Currents on Arteries
External Duodenal Fistula
Acute Suppurative and Ruptured Appendicitis
Recurrent Fibromatous Tumors of the Skin
Localization and Removal of Foreign Bodies from the Tissues
Spasm of the Ileum Simulating Regional Ileitis
Operations for Inguinal and Femoral Hernias
Technique for Amputations Through the Thigh
Intestinal Changes and Splanchnic Circulation in Shock
Production of Normoblastic Crises in Splenectomized Rats
Reaction of Tissues to Suture Materials
Postoperative Laryngeal Edema
Pulley Stitch for Sliding Hernia Operation

With this wealth of experience, Dr. Willis should be a valuable help to the students of The Chicago Medical School.

Donald H. Atlas, M.D., Ph.D.

Dr. Atlas was born in Chicago in 1913. He received his pre-medical and medical education at Northwestern University and was graduated from the Medical School in 1937. Prior to that he was the Rockefeller Foundation Fellow at the Institute of Neurology from 1934 to 1936, working in the laboratory of the late Dr. S. W. Ranson. In 1936 he received his M.S. degree in Neurology. The following year, after receiving his M.D. degree, he worked as an assistant in Pathology in the laboratory of the late Dr. R. H. Jaffe at Cook County Hospital. He interned at Cook County Hospital from 1938-1939, and then until 1940 he spent his time as a resident in Medicine at the Mt. Sinai Hospital of Chicago. In 1940 he returned to Northwestern University Medical School as the Macy Foundation Research Fellow in Medicine. Dr. Atlas received his Ph.D. degree in Medicine from Northwestern University Medical School in 1942. During the next forty-three months he served in the Army and was stationed in Alaska and the Aleutian Islands. As member of the United States Army he rose in rank from lieutenant to major. In 1945 he became a Diplomate of the American

Dr. Donald H. Atlas

Board of Internal Medicine. Dr. Atlas has been an associate attending physician at Cook County Hospital and member of the medical staff of Mt. Sinai Hospital since 1941. He was also an instructor in Medicine at Northwestern University Medical School prior to his military service. For two years following and one year prior to his military career, Dr. Atlas was engaged in private practice and became an associate member of the American College of Physicians. We now wish to welcome Dr. Atlas as a full-time Assistant Professor in Medicine of The Chicago Medical School.

His publications include:

The Afferent Path of the Pupillary Light Reflex in the Monkey. Brain, vol. 49, p. 234, 1936.

Associated Facial, Vocal and Respiratory Components of Emotional Expression. J. Neur. & Psychopath., vol. 17, p. 241. 1937.

Topography of the Brain Stem of the Rhesus Monkey, with Special Reference to the Diencephalon. J. Com. Neur., vol. 66, no. 1. 1937

Anatomy of the Pretectal Area, ibid. 1937.

Acute Perforation of Lymphosarcomatous Ulcer of the Stomach. Annals of Surgery, Dec. 1941.

Biologic False Positive Reactions for Syphilis Associated with Hyperproteinemia. Arch. Derm. & Syph., vol. 46, p. 713, Nov. 1942.

A Note on the Use of the Kagan Falling Drop Proteinometer Tech. Bull. of Registry of Med. Tech., vol. 4, no. 2. 1943.

Incidence and Cause of Hyperproteinemia. Arch. of Int. Med., vol. 71, p. 377, March 1943.

Marked Hyperproteinemia in Subacate Bacterial Endocarditis. Illinois Medical Journal, vol. 91, no. 2, February 1947.

Herman L. Eisenberg, B.S., M.D.

A new addition to the full-time Clinical Medicine staff of The Chicago Medical School is Dr. Herman L. Eisenberg, as instructor.

Born in 1918, Dr. Eisenberg was graduated from the University of Wisconsin Medical School in 1943, and went directly from there to Mt. Sinai Hospital for his internship.

From 1943 to 1946, Captain Eisenberg served as a Battalion Surgeon in the Army. After this period of military experience, Dr. Eisenberg returned to Mt. Sinai Hospital to begin a three-year residency in Medicine. It was during this time that Dr. Eisenberg became acquainted with the students and staff of The Chicago Medical School and it has been an easy transition for him to become a full-time member of the CMS faculty.

Dr. Herman L. Eisenberg

Allan E. Sachs, M.D.

We wish at this time to welcome Dr. Allan E. Sachs, who has joined the full-time staff of The Chicago Medical School, as Assistant Professor of Surgery.

Dr. Sachs received his Bachelor of Science degree in 1934 and his M.D. from the University of Chicago, Rush Medical College in 1937. The following two years were spent at Michael Reese Hospital as interne and house surgeon and then, until 1941, he was on the surgical staff of the Veterans' Hospital in San Francisco, California. The following year he was a surgical resident at Michael Reese Hospital and in 1942 he became an assistant in Pathology at the University of

Dr. Allan E. Sachs

Michigan Medical School. In 1942, Dr. Sachs entered the U. S. Medical Corps from which he was retired the following year. He then engaged in private practice, was on the clinical staff in Surgery at the Michael Reese Hospital, and was an assistant in Anatomy at the University of Chicago. In 1944 he was made a member on the Advisory Board in Surgery to Selective Service; in 1946 he became a Diplomate of the American Board of Surgery; and in 1947, a Fellow of the American College of Surgeons. At present Dr. Sachs is an associate in Surgery at Cook County Hospital, and he is also an Adjunct in Surgery at Mt. Sinai Hospital. Dr. Sachs' publications include papers on Septicemia, Osteomyelitis, Skin Grafting, Appendicitis, and Popliteal Hernia.

Nathan Flaxman, B.S., M.D.

Another addition to the full-time Clinical Medicine staff of The Chicago Medical School is Nathan Flaxman, B.S., M.D., as Associate in Medicine.

Dr. Flaxman is a native of Chicago and received his professional training at Loyola Medical School, from which he graduated in 1930. The doctor served two periods of internship, one at Columbus Hospital from 1930-1931, and another at Cook County Hospital the following year. From 1932 until last year, Dr. Flaxman taught medicine at Loyola Medical School.

His varied professional activities have included such posts as Associate Attending Physician at Cook County Hospital (1939-1947); Associate in Medicine, Mount Sinai Hospital (1933-present); Chief of Staff, Manor Hospital; and Chief of Clinics, Mount Sinai Hospital.

During the last war, Dr. Flaxman served as Civilian Physician, Chest Section, Medical Unit No. 1, at the Armed Forces Induction Center in Chicago from 1943 to 1944.

Dr. Nathan Flaxman

Dr. Flaxman is a member of the Chicago Medical Society and a Fellow of the American Medical Association. His main fields of research have been Cardiology and the History of Medicine and, since 1934, he has had published fifty articles on these subjects.

Harry C. Rolnick, M.D.

Dr. Harry C. Rolnick has recently been appointed Professor and Chairman of the Department of Genito-Urinary Surgery of The Chicago Medical School.

A product of the Chicago educational system, Dr. Rolnick graduated from the Northwestern University Medical School in 1911. Almost immediately after finishing his internship at Cook County Hospital, the doctor accepted a teaching position at his Alma Mater which he retained until 1927. He also taught at Loyola University as Clinical Professor of Urology (1929-1935); and from 1938 to 1948 he returned to the faculty of Northwestern Medical School as Associate Professor of Urology.

Dr. Rolnick served in World War I as Urologist for the 42nd (Rainbow) Division of the Army.

A former president of the Chicago Urological Society, Dr. Rolnick is a member of the American Board of Urology, the American College of Surgeons, the Institute of Medicine, and the International College of Surgeons.

Many of Dr. Rolnick's articles, dealing with various clinical and experimental subjects, have been published in the professional journals, but perhaps the doctor is best known as the author of the textbook, "Urology," which was first published in 1928 and is soon to be brought out in its fifth edition.

Dr. Harry C. Rolnick

Russell V. Millisir, Ph.D., M.D.

Dr. Millisir was born on February 27, 1906, in Rochester, Indiana. He received his B.A. degree from DePauw University in 1928 and from then

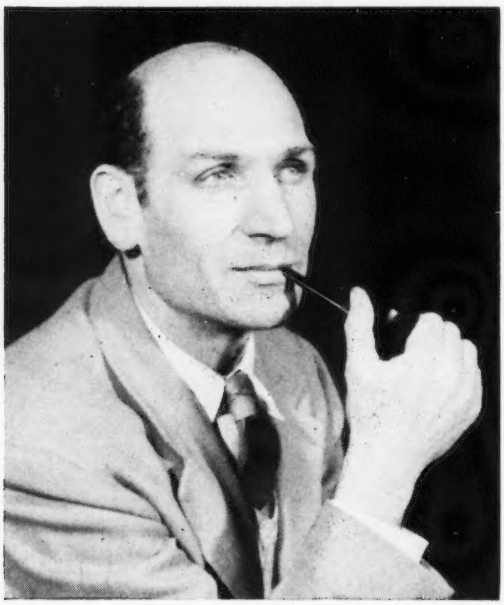
Dr. Russell V. Millisir

until 1931 served as an instructor in Anatomy at Cornell University Medical School. The following year he served again as an Anatomy instructor but changed his locale to Northwestern University Medical School. In 1932, Dr. Millisir came to The Chicago Medical School where he remained until 1937 as an assistant professor of Anatomy. The year he left The Chicago Medical School he received his Bachelor of Medicine degree from Northwestern, and after a year's internship at White Cross Hospital in Columbus, Ohio, received his M.D. degree in 1938. Following this he spent one year at the White

Cross Hospital as a resident in Pathology. In 1939 he joined the staff of the Ohio State Medical School as an instructor in Pathology, and in 1945 was promoted to assistant professor in Pathology, which position he held until 1948. In 1947, Dr. Millisir was certified by the American Board in Pathology. He is a member of the Ohio State Medical Society, the Ohio Society of Pathologists, and the American Medical Association. At this time we wish to welcome Dr. Millisir back to The Chicago Medical School where in July 1948 he assumed the position of associate professor in Pathology.

A. Robert Goldfarb, M.S., Ph.D.

Dr. Goldfarb, a native of Philadelphia, has joined our Biochemistry Department as instructor, and we, of The Chicago Medical School, want to



Dr. A. Robert Goldfarb

welcome him to his new position. Dr. Goldfarb received his B.S. degree in 1928 from the College of the City of New York. In 1931 he received his Master's degree from the University of Chicago, and in 1935 his Ph.D. from New York University. When his school days were over, Dr. Goldfarb spent some time in industrial research, and from this point he went on to become Chief Chemist at the Brooklyn Jewish Hospital. He is a member of the American Chemical Society, Sigma Xi, and the New York Academy of Science. His publications have been in the fields of biochemistry, organic chemistry, and physical organic chemistry.

Ben B. Blivaiss, M.S., Ph.D.

The pre-clinical staff of The Chicago Medical School is continually augmented, and among the newest additions is Dr. Ben B. Blivaiss, instructor in Physiology. Dr. Blivaiss received his Bachelor's degree, his Master's degree, and his Ph.D. from the University of Chicago. While a graduate student he was a Laboratory Instructor in Anatomy and Embryology in the A.S.T.P. program, Research Phramacologist at the Toxicity Laboratory of Chemical Warfare Service, and Principal Investigator for the Committee on Growth of the National Research Council and the American Cancer Society.

After receiving his Doctorate in 1946, Dr. Blivaiss went to the University of Illinois at Urbana, Illinois, as an Instructor in Physiology. For the past year he has been Guest Investigator at the University of Chicago. He is primarily interested in Endrocrinology, especially hormone interrelations, the relation of endocrines to reproduction, the relation of hormones to pigmen-

Dr. Ben B. Blivaiss

tation, and also the effect of gonadal hormones in mating behavior.

Dr. Blivaiss is a member of the American Association for the Advancement of Science, the American Society of Zoologists, and of Sigma Xi.

His publications include the following; and many others on related subjects too numerous to mention:

Blivaiss, B. B. 1946. Modifications in feather growth rate of thyroidectomized Brown Leghorn roosters following adminstration of thyroxin and estrogen. Anat. Rec. 94 (Suppl.): 21.

1946. Modifications in plumage pattern of thyroidectomized roosters following estrogen administration. Anat. Rec. 94 (Suppl.): 43.

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1947. Interrelations of thyroid and gonad in the development of plumage and other sex characters in Brown Leghorn rooster. Ph.D. Thesis. Physiol. Zool. 20: 67-107.

1947. Development of secondary sexual characters in thyroidectomized Brown Leghorn hens. Jr. of Exper. Zool. 104: 267-310.

Response of secondary sexual characters in thyroidectomized Brown Leghorn hens to hormone therapy. (Prepared for publication.)

Alumni News

1933

Dr. Pak Keung Chan writes that he would like to correspond with some of his classmates. His address is Rua Das Estalagens, 79 Macau, China.

1937-38

Dr. Anton Wellstein has been elected president of the Henry County Medical Society, Henry, Illinois.

1941

Dr. John M. Staron has been elected secretary-treasurer of the Jackson Park Branch of the Chicago Medical Society. In addition, Dr. Staron has become a member of the American Association of Industrial Physicians and Surgeons.

1943

We are pleased to hear of Dr. and Mrs. Saul Nichterns' new future doctor, named David Matthew — weight 8 lbs. 4 oz.

We were pleased to note Dr. Berton J. Winston's excellent article in the April 1948 issue of the Illinois Medical Journal. It is entitled "Hydatiform Mole with Eclampsia Occurring in the Fourth Month of Pregnancy."

Dr. Arnold L. Berger announced the opening of his office at 51 Plainfield Avenue, Floral Park, Long Island, N. Y.

Dr. Walter Greenson also announced the opening of his office in Toledo, Ohio. He is limiting his practice to Dermatology.

1944

It is with great pleasure that we announce Dr. Max N. Silber's return from military service and the opening of his office at 1200 North Dearborn Parkway, Suite 8, Chicago 60, Illinois.

1945

Dr. Arthur D. Sincoff announced the opening of his office at 1111 Park Avenue, New York 28, N. Y.

1946

Dr. and Mrs. Bernard Z. Reizner proudly tell us about their new addition, Kenneth Mitchell, 7 lbs. 6 oz.

1947

Mr. and Mrs. I. L. Silverman announce the marriage of their daughter, Francine, to Dr. Jerome A. Ehrlich on Sunday, May 9, 1948. Best wishes to you both.

Social Notes

Two more married couples will be added to the sophomore class when Maurice J. Sherman exchanges vows with Bobette Norton on September 19, and Melvin Ehrich says "I do" to Leah Isaacson on July 2 . . . That'll make 27 "ball-and-chainers" in the Class of '50 . . . Tina and Joseph Vesce joined the "Honey, I Love You" Club on June 27 . . . The Wayne Hiltons celebrated their first anniversary on July 27 . . . Ditto for Muriel and Seymour Filman on August 24 . . . Two-year men included Evelyn and Marvin Wertheim on May 30 and Florence and Lawrence Moser on September 1 . . . Keep your chins up, the first 100 years are the hardest! . . . Florence and David Spiegal are getting an application for the Class of 1974 for their youngster expected in February.

With deserving acclaim for his superb and efficient leadership, Vernon Phillips was re-elected as president of the Freshman Class for the coming year. His unanimous election is no doubt due, in no small measure, to the entertaining and popular class meetings last year. Bert Carnow was likewise unanimously re-elected as vice-president. Ann Nelson was elected class secretary; Kiku Morimoto, also unanimously re-elected treasurer.

WEDMEDS

With the married student at C.M.S. becoming less of a rarity, there has arisen an organization to satisfy the needs of not only the student, but his better half. This organization, dubiously entitled the "Wedmeds," has attempted to form a social outlet for these married couples.

The "Wedmeds" have enjoyed many activittes this year, including a dinner, highlight of which was a speech by Dr. Jordon of the Psychiatry department, a "Dungaree" night, wiener roast, beach party, and numerous other social events, and are now planning an outing at the Dunes.

Plans are on the fire for bringing the Freshmen into the organization by having a meeting for them in the early part of October. The group will also sponsor an all-school dance sometime in the winter.

With Cupid being kept busy getting more "Meds" to wed, the "Wedmeds" will find themselves an integral part of the social scene.

The Role of Physicians

Doctors came to see her singly and in consultation, talked much in French, German and Latin, blamed one another, and prescribed a great variety of medicines for all the diseases known to them, but the simple idea never occurred to any of them that they could not know the disease Natasha was suffering from, as no disease suffered by a live man can be known, for every living person has his own peculiarities and always has his own peculiar, personal, novel, complicated disease, unknown to medicine — not a disease of the lungs, liver, skin, heart, nerves and so on mentioned in medical books, but a disease consisting of one of the innumerable combinations of the maladies of these organs.

This simple thought could not occur to the doctors (as it cannot occur to a wizard that he is unable to work his charms) because the business of their lives was to cure, and they received money for it and had spent the best years of their lives on that business. But above all, that thought was kept out of their minds by the fact that they saw they were really useful, as in fact they were to the whole Rostov family. Their usefulness did not depend on making the patient swallow substances for the most part harmful (the harm was scarcely perceptible as they were given in small doses), but they were useful, necessary and indispensable because they satisfied a mental need of the invalid and of those who loved her — and that is why there are, and always will be pseudo-healers, wise women, homeopaths and allopaths. They satisfied that eternal human need for hope of relief, for sympathy, and that something should be done, which is felt by those who are suffering.

From Count Leo Tolstoy, *"War and Peace,"* Book XI, Chapter 16.

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Pre-partum Hemorrhage—

(Continued from page 25)

avoided if cross-matching and typing of all obstetrical patients early in pre-natal care were performed.

SUMMARY

A brief diagnostic picture of the more frequent causes of pre-partum hemorrhage is presented as well as summaries of the modern concepts of treatment. The gestation period is divided into three trimesters and each pathological condition is discussed under the period during which it most commonly occurs. It is emphasized that proper understanding of these various causes for bleeding is essential in the reduction of both morbidity and mortality to the mother and to the developing fetus.

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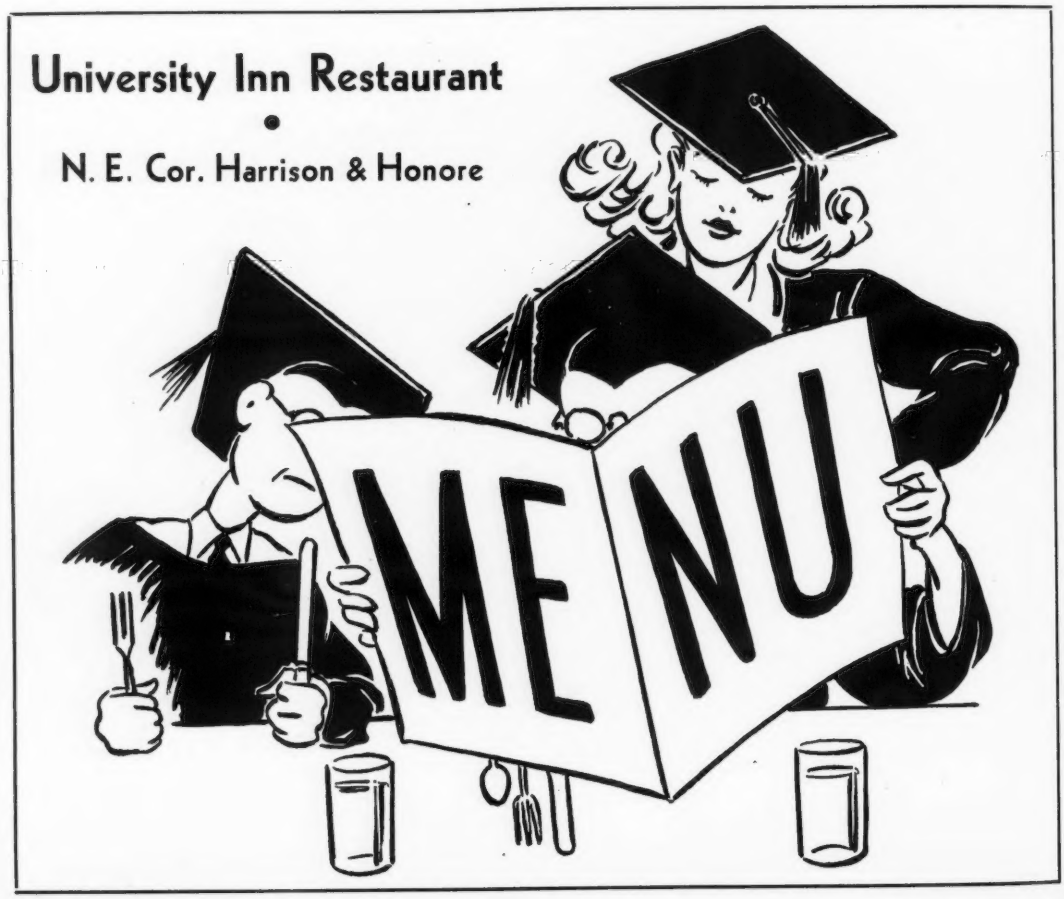

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